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(54) Title: DEVELOPMENT OF THERAPEUTICS FOR THE TREATMENT OF ENDOTOXIN-MEDIATED DISEASES

(57) Abstract: The subject invention comprises a method for identifying an evolutionarily meaningful nucleotide change in a primate's *TLR4* polynucleotide. It further comprises methods for identifying agents that interact with the corresponding evolutionarily meaningful amino acid change so as to modulate the function of the *TLR4* polypeptide, thereby attenuating activation of the NF- κ B pathway. Such agents are useful in mitigating the LPS mediated response and in the treatment of sepsis, severe sepsis and septic shock.

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